10/509323

PCT/JP2003/004433

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DK-219-X-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/004433	International filing date (*day/month/year*) 08 April 2003 (08.04.2003)	Priority date (*day/month/year*) 08 April 2002 (08.04.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 38/08, 31/65, 31/7036, 47/36, 47/38, 9/06, 9/16, 9/70, A61P 19/00, 19/02, 31/04		
Applicant DENKI KAGAKU KOGYO KABUSHIKI KAISHA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30 September 2003 (30.09.2003)	14 May 2004 (14.05.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/004433

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELI[redacted]ARY EXAMINATION REPORT

International application No. [redacted]CT/JP03/04433

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	8, 9, 12	YES
	Claims	1-7, 10, 11, 13, 14	NO
Inventive step (IS)	Claims		YES
	Claims	1-14	NO
Industrial applicability (IA)	Claims	1-14	YES
	Claims		NO

2. Citations and explanations

Document 1: WO 93/20858 A (FIDIA S.P.A.) October 28, 1993
Document 2: JP 7-157439 A (Eisai Co., Ltd.) June 20, 1995
Document 3: JP 60-87219 A (Merck Patent GmbH) May 16, 1985
Document 4: WO 99/15150 A1 (BUFORD BIOMEDICAL, INC.) April 1, 1999
Document 5: EP 147021 A1 (ED. GEISTLICH SOHNE A.G. FUR CHEMISCHE INDUSTRIE) July 3, 1985
Document 6: US 5709875 A (LEBUGLE, Albert) January 20, 1998
Document 7: JP 4-327525 A (Kyocera Corp.) November 17, 1992
Document 8: JP 2000-230002 A (Denki Kagaku Kogyo K.K.) August 22, 2000

Novelty

Claims 1-7, 10, 11, 13 and 14

Document 1 describes a bone replacement preparation that contains a hyaluronic acid ester and various antibacterial substances such as gentamycin, streptomycin, erythromycin, or kanamycin, etc., and it states that infections do not occur when this preparation is used (page 3, lines 25 to 34; Examples 1 to 37).

As a result, the inventions of claims 1-7, 10, 11, 13 and 14 are described in document 1, and therefore lack novelty.

Claims 1-6, 13, and 14

Document 2 describes a preparation for the treatment of infections following surgery for osteomyelitis and bone fractures that is characterized by the fact that it contains polymer substances such as chondroitin sulfate and hyaluronic acid, etc., and an antibiotic (claims 1-5; Par. Nos. 0002, 0003, 0007 and 0010). In the Examples, a preparation containing gentamycin and sodium chondroitin sulfate is described (Example 1).

As a result, the inventions of claims 1-6, 13 and 14 are described in document 2, and therefore lack novelty.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

Document 3 describes a preparation containing an antibiotic such as gentamycin, etc., and acidic polysaccharides (claims 1-5), and it states that this preparation is preferably used for the topical treatment of bone infectious disease (page 5, upper right column, lines 7 and 8). In addition, Example 1 describes a preparation that contains gentamycin and sodium pectinate.

As a result, the inventions of claims 1-6, 13 and 14 are described in document 3, and therefore lack novelty.

Claims 1-7 and 14

Document 4 describes a drug delivery system for use in the treatment of infections such as osteomyelitis that contains an anti-infection agent such as gentamycin and polysaccharides such as hyaluronic acid and chondroitin sulfate, etc. (page 1, lines 8 to 10; page 16, line 27 to page 17, line 9). In addition, Examples 1-10 describe delivery systems in which hyaluronic acid, dextran, or chondroitin sulfate is formulated with norfloxacin, cefazolin, penicillin, etc.

As a result, the inventions of claims 1-7 and 14 are described in document 4, and therefore lack novelty.

Claims 1-5 and 14

Document 5 describes a medicinal composition for use in the treatment of osteitis and osteomyelitis that contains an antibacterial substance and dextran (claims 6 and 8). In addition, Examples 4-8 describe medicinal compositions that contain taurolidine or taurultam and dextran.

As a result, the inventions of claims 1-5 and 14 are described in document 5, and therefore lack novelty.

Claims 1-5, 13 and 14

Document 6 describes a transplantation material that will not be accompanied by infectious disease such as osteomyelitis, etc., when promoting the formation of bone that contains netilmicin or gentamycin and dextran (column 2, lines 1 to 16; Examples 3 to 11).

As a result, the inventions of claims 1-5, 13 and 14 are described in document 6, and therefore lack novelty.

Claims 1-5 and 14

Document 7 describes a pharmaceutical preparation that is used in the treatment of osteomyelitis, etc., that contains chitin and kanamycin or chitosan and tetracycline (Par. No. 0001, Examples 1-3).

As a result, the inventions of claims 1-5 and 14 are described in document 7, and therefore lack novelty.

Inventive Step

Claims 1-8, 13 and 14

This examination finds that cellulose derivatives such as carboxymethyl cellulose were commonly used as a polysaccharide for carrying active ingredients in the field of drug delivery before the filing of this application, and therefore persons skilled in the art could easily conceive of using them in place of the polysaccharide described in documents 1-7.

In addition, in looking at the Detailed Description of the inventions of this application, this examination finds no particularly outstanding effect in specifying the polysaccharide that could not be predicted by persons skilled in the art from the descriptions in documents 1-5 and widely known technology.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

Claims 1-7 and 9-14

Document 1 describes a composition for use in the treatment of bone infectious diseases that contains a hyaluronic acid ester and an antibiotic.

Document 8 describes a hyaluronic acid gel with a molecular weight of 800,000 or higher as a biocompatible material for use in bone restoration, etc. (claims 1-4; Par. Nos. 0011 to 0013).

This examination finds that it was conventional practice for persons skilled in the art to replace a certain ingredient with another ingredient having the same function in the field of pharmaceutical formulation before the filing date of this application, and documents 2 and 4, etc. describe the selection and use of a preferable matrix polymer as needed. Therefore, persons skilled in the art could easily conceive of using the crosslinked hyaluronic acids described in document 1 or document 8, or another crosslinked hyaluronic acid in place of the polysaccharides described in documents 1-7.

In addition, in looking at the Detailed Description of the inventions of this application, this examination finds no particularly outstanding effect in specifying the structure of the hyaluronic acid that could not be predicted by persons skilled in the art from the descriptions in documents 1-8.